U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

Current approaches to quantify ultra-low (part per billion) levels of elements in foods

Patrick J. Gray
patrick.gray@fda.hhs.gov

FDA Center for Food Safety and Applied Nutrition
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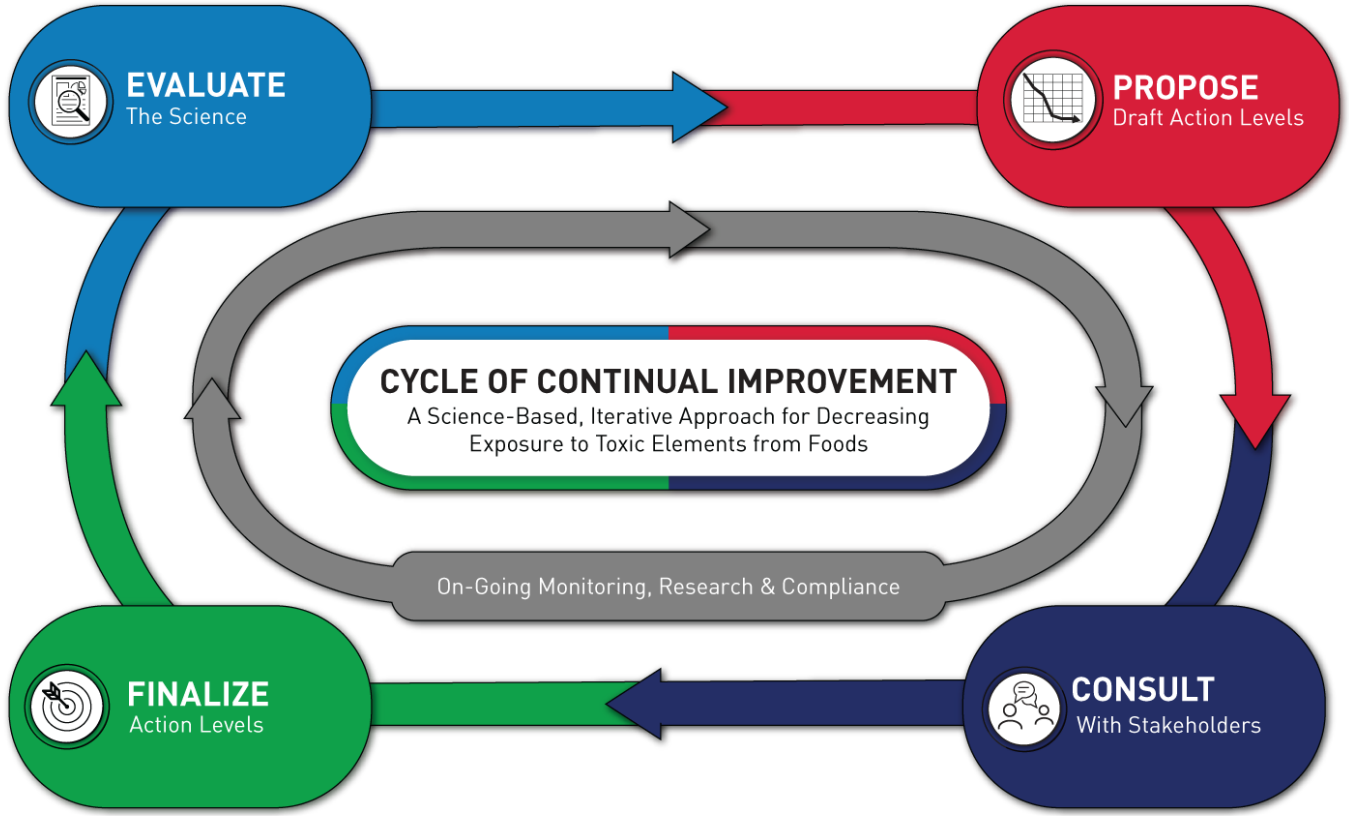
FDA Closer to Zero Action Plan

analytical methods and data collection are involved in all 4 stages of the Closer to Zero Plan



data driven, science backed action levels require measurement at part per billion levels

Elemental Analysis: MW ICP-MS

1. Homogenize foods

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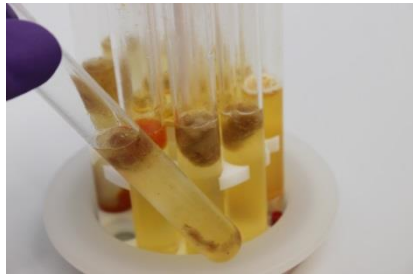
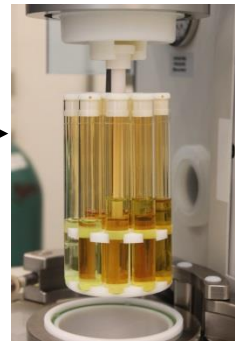
2. Decompose (digest) in microwave



HNO_3, H_2O_2

Heat



dilute

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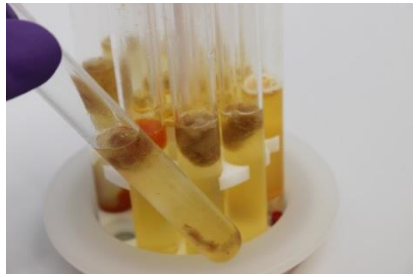

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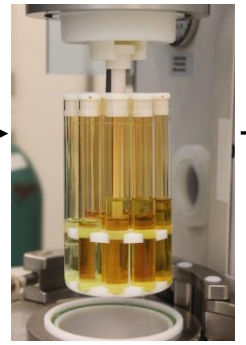
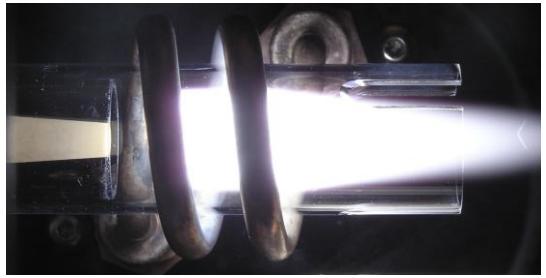


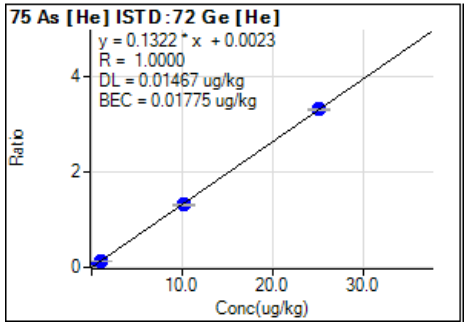
dilute

3. Analyze by ICP-MS



aspirate

count



external calibration

x dilution factor

Answer!

Limit of Quantification

$$LOQ_{food} = LOQ_{test\ solution} \times Dilution\ Factor$$

$LOQ_{test\ solution}$= Analytical solution quantification limit (ASQL)

Limit of Quantification

$$LOQ_{food} = LOQ_{test\ solution} \times Dilution\ Factor$$

$$LOQ_{food} = ks \times \frac{final\ mass}{digest\ mass}$$

final digest dilution mass, typically 50 g

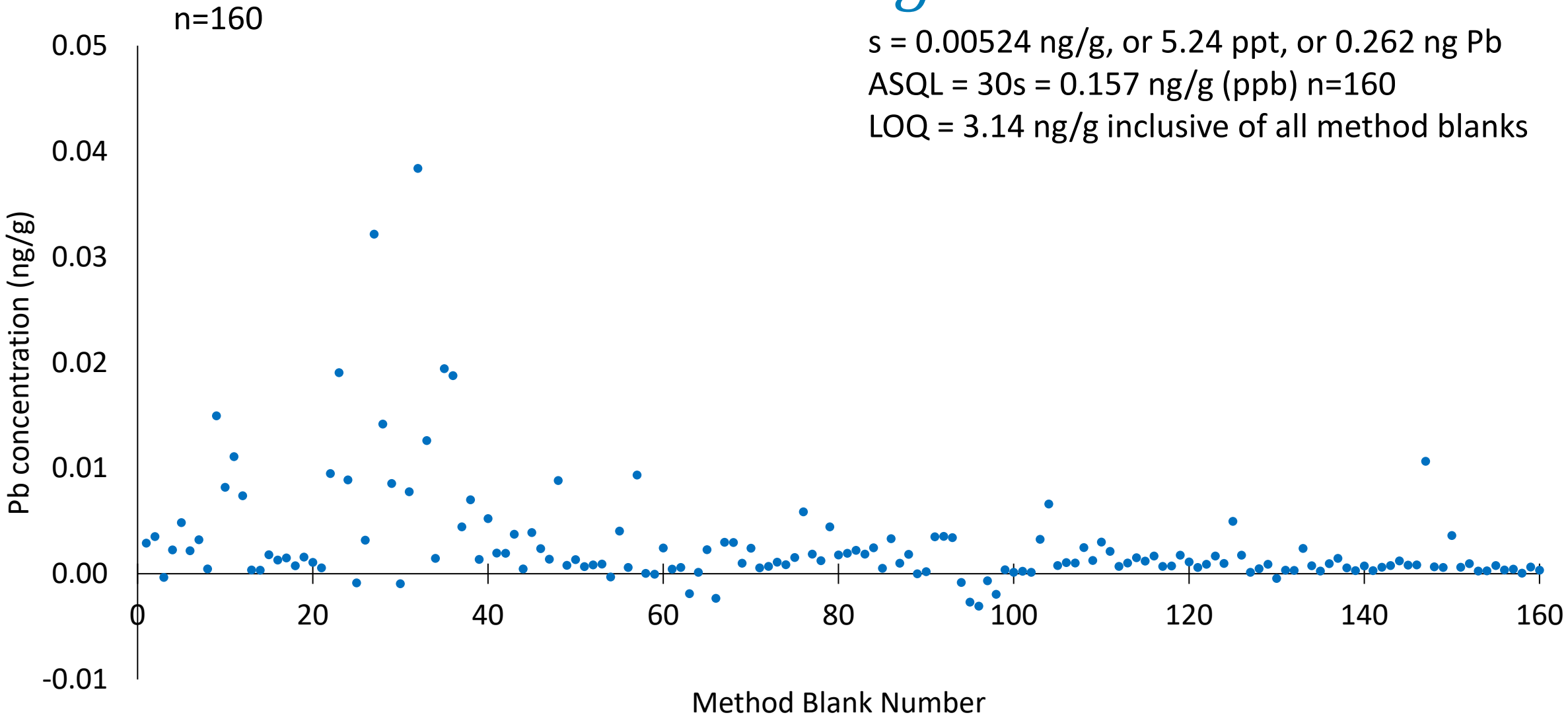
k is a coverage factor, often 10
FDA uses k = 30

s is the standard deviation of method blanks

amount of food digested (g), typically 0.5 g for dry foods, up to 2-3 g for baby foods

$LOQ_{test\ solution}$= Analytical solution quantification limit (ASQL)

$$LOQ_{food} = ks \times \frac{final\ mass}{digest\ mass}$$



s = 0.00524 ng/g, or 5.24 ppt, or 0.262 ng Pb
ASQL = 30s = 0.157 ng/g (ppb) n=160
LOQ = 3.14 ng/g inclusive of all method blanks

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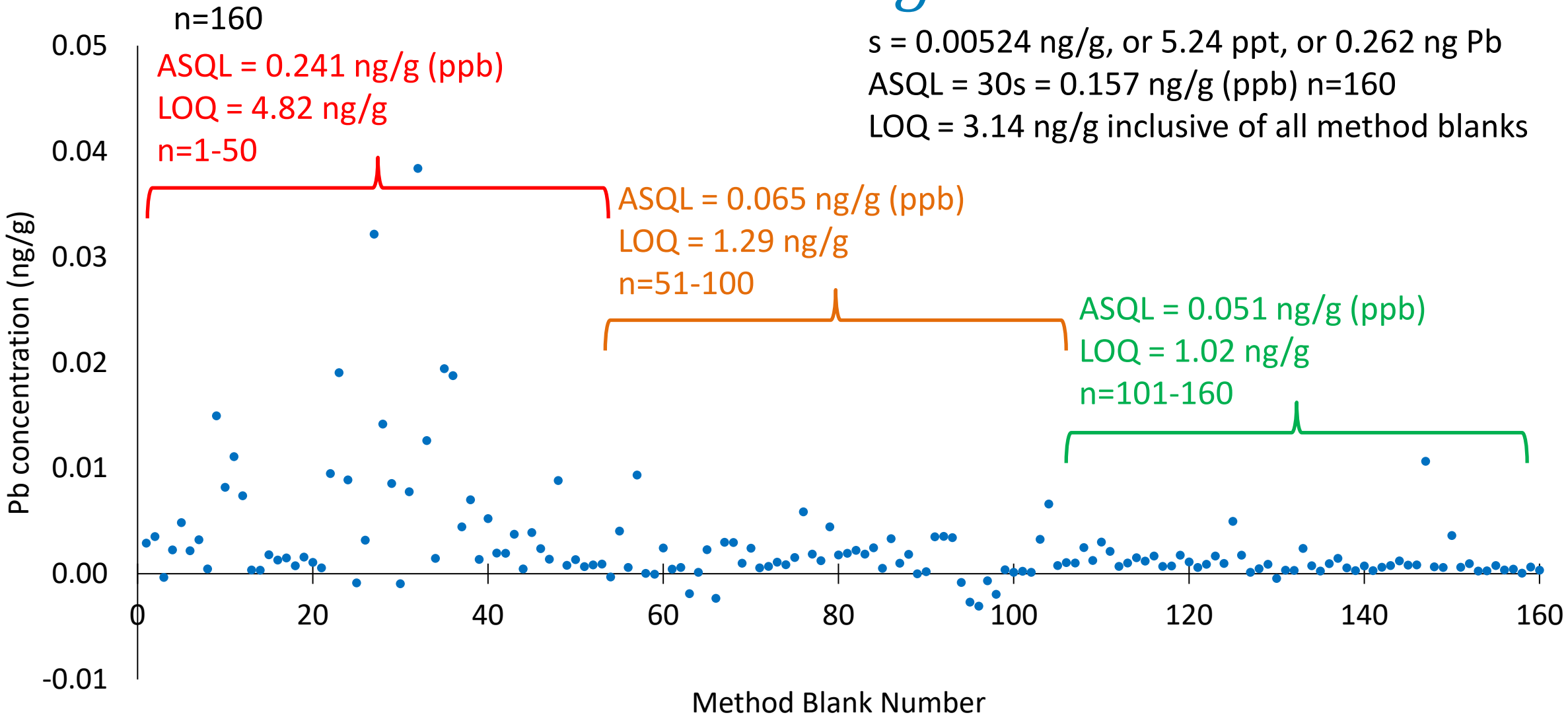


Limit of Quantification

Detection and Quantification limits are determined by the **spread** of **method** blank values

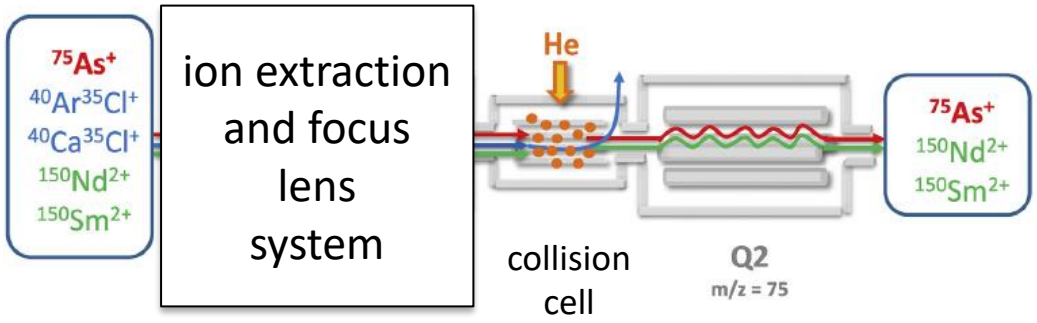
Blank values vary due to contamination

- Reagent contamination (e.g. dirty, low purity acids) are uniform
- It would be easy to subtract a **consistent** contamination

Contamination in elemental analysis is dominated by microwave vessels (unpredictable carryover)

What about $$$ instruments?

Single Quad ICP-MS ($)



He collision gas mitigates polyatomic interferences

Triple Quad ICP-MS ($$$)

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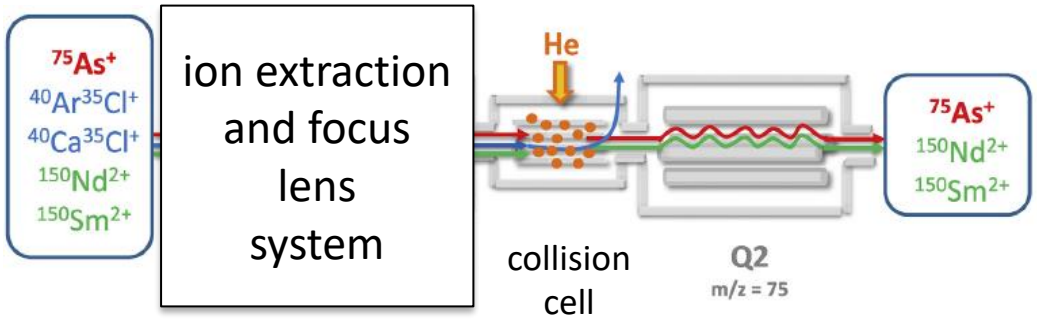

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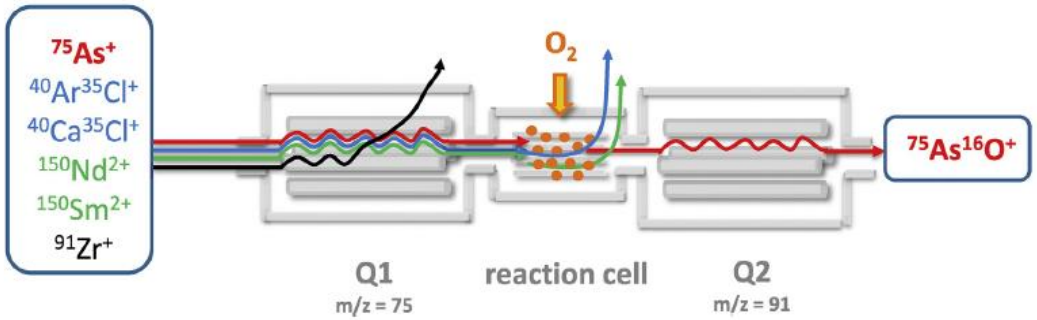

Reaction gas (O_2) selectively reacts with interferences

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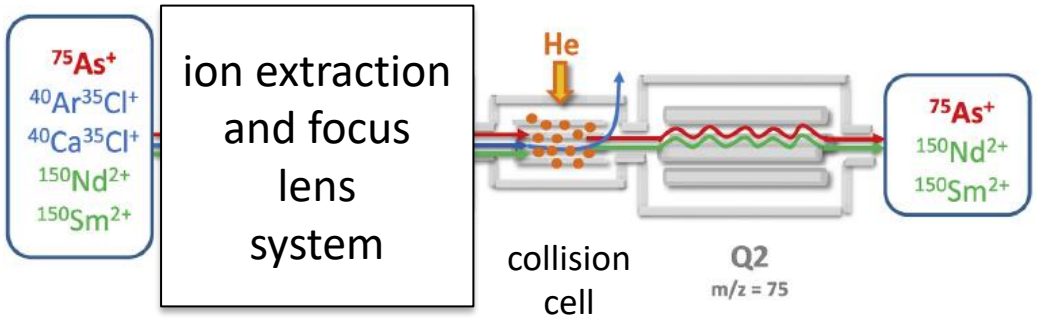

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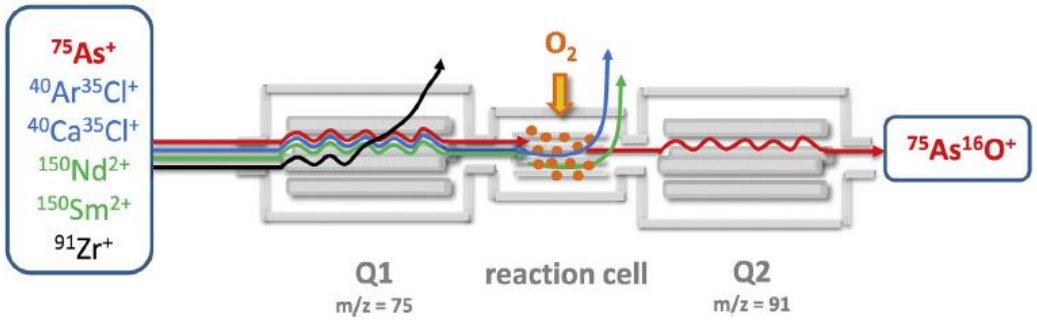


Reaction gas (O_2) selectively reacts with interferences

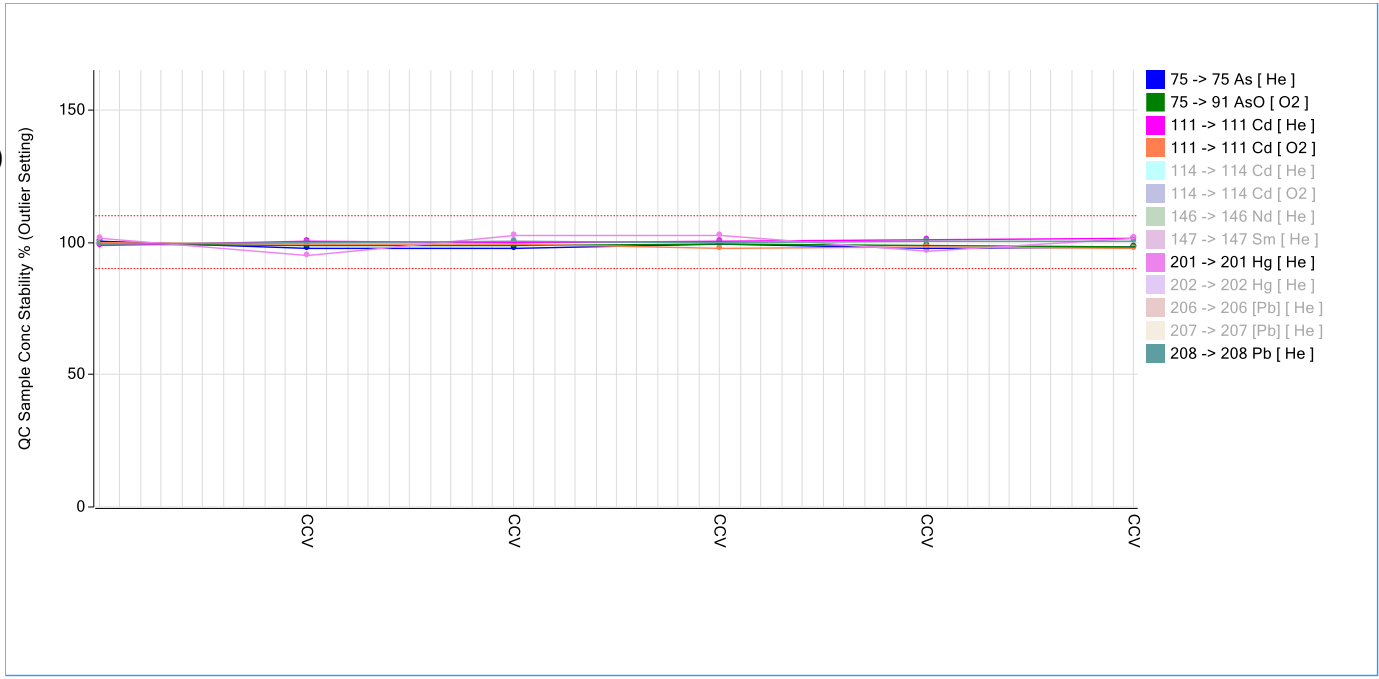
ASQL (30s), n=148	Interference	ICP-MS (KED)	ICP-QQQ
^{75}As	$^{40}Ar^{35}Cl^+$	0.117 ng/g	0.108 ng/g
^{111}Cd	$^{95}Mo^{16}O^+$	0.057 ng/g	0.052 ng/g

ICP-QQQ shows no improvement. Interferences are sufficiently mitigated by KED. LOD/LOQ determined by blank contamination

FDA EAM 4.7 Quality Controls

Required Quality Controls

Internal Standard recovery	60-120%
Stability check (mid-level std)	< 10% RSD
Calibration Curve	R > 0.995
Initial Calibration Verification (2nd source)	± 10%
Continuing Calibration Blank	< ASQL
Continuing Calibration Verification	± 10%
Reference Material	± 20%
Fortified Analytical Portion	± 20%
Fortified Analytical Solution	± 10%
Duplicate Portions	< 20% RPD

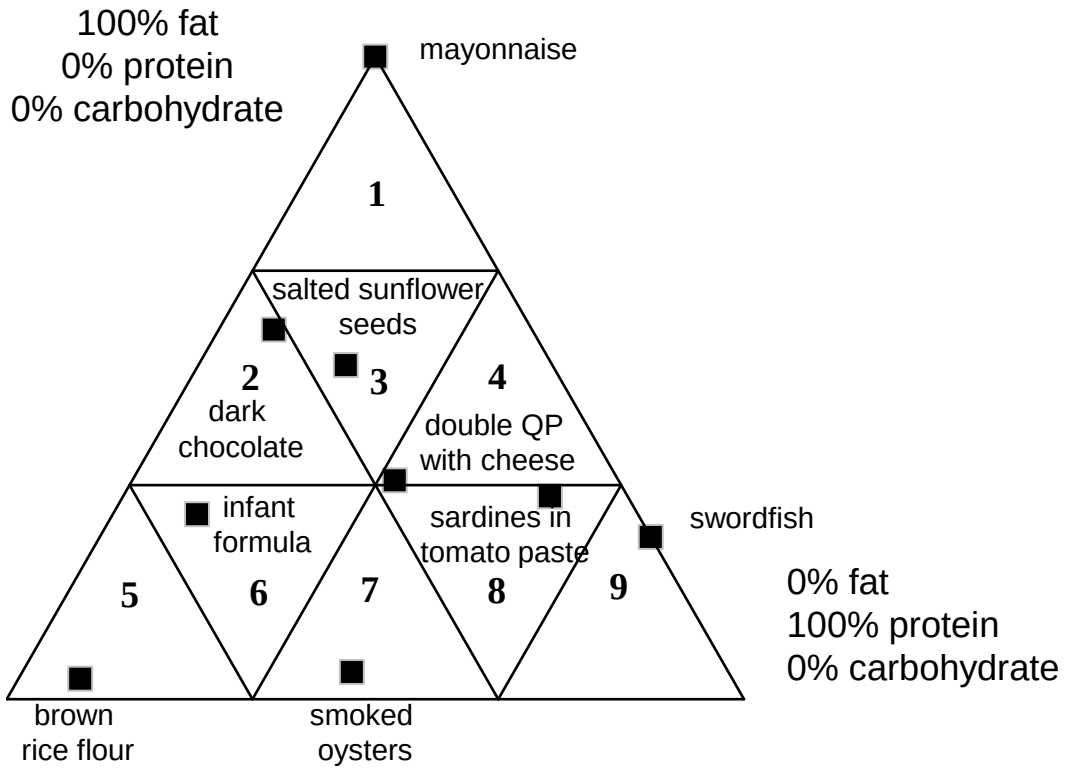


Expanded uncertainty better than ± 15% when concentration > LOQ

FDA EAM 4.7 Validation

Validated in food matrices spanning food composition triangle

Used by FDA, USDA, state lab partners, and some contract laboratories



590 GRAY & CUNNINGHAM: JOURNAL OF AOAC INTERNATIONAL VOL. 102, No. 2, 2019

RESIDUES AND TRACE ELEMENTS

Inductively Coupled Plasma Collision Cell Quadrupole Mass Spectrometric Determination of Extractible Arsenic, Cadmium, Chromium, Lead, Mercury, and Other Elements in Food Using Microwave-Assisted Digestion: Results from an FDA Interlaboratory Study

DOI: https://doi.org/10.5740/jaoacint.18-0129

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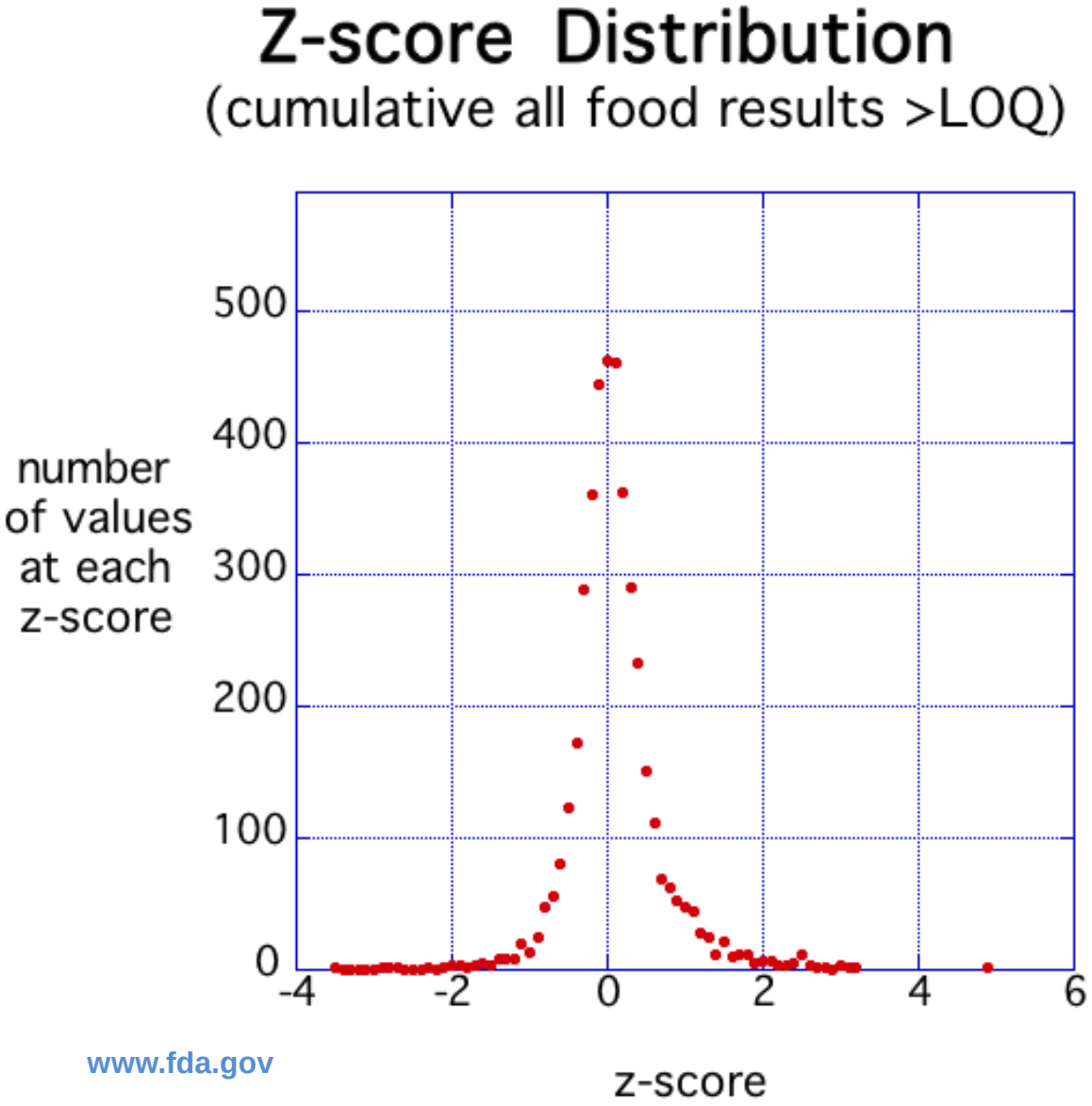

Total 4206 food analysis results above LOQ

Normal random distribution (Gaussian fit R=0.99)

93.1% of results -1 < z < +1

98.5% of results -2 < z < +2

99.4% of results -4 < z < +4

AOAC methods

FDA EAM 4.7	AOAC 2013.06	AOAC 2015.01
MLV in across all food groups		
LODs (for baby foods)		
As: 0.25 µg/kg (ppb)		
Cd: 0.15 µg/kg (ppb)		
Pb: 0.35 µg/kg (ppb)		
Hg: 0.08 µg/kg (ppb)		

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AOAC 2013.06

MLV in carrot, fish, mushroom, wheat, shellfish

LODs

As: 60 µg/kg (ppb)

Cd: 30 µg/kg (ppb)

Pb: 40 µg/kg (ppb)

Hg: 90 µg/kg (ppb)

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AOAC methods

FDA EAM 4.7

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AOAC 2015.01

SLV* in infant formula, chocolate, rice flour, fruit juice

LODs

As: 4 µg/kg (ppb)

Cd: 2 µg/kg (ppb)

Pb: 8 µg/kg (ppb)

Hg: 6 µg/kg (ppb)

* not multi-lab validated

Conclusions

Detection and Quantification limits (LOD/LOQ) are determined by the **spread** of **method** blank values

Effort required to quantify low ppb As, Cd, Pb, Hg

Validated methods needed to support Closer to Zero effort


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